ON THE SURGICAL DISSEMINATION OF CANCER.[1]

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THE subject in question, not being mentioned by the authors of text-books on general and special surgery, and unknown in periodical literature, seems of sufficient importance to deserve consideration. The present essay is an *a priori* consideration of a possibility or probability occurring in the course of the development and treatment of cancer; an outline of a train of thought based on clinical observation, that may deserve more extensive study in the future.

The subject-matter itself is not strictly new, observations bearing upon it having been made and published from time to time in an unconnected manner. The leading idea of this essay was originated in the year 1877 by observing the course of a striking case of rapid dissemination of cancer. Since then a number of other cases have accumulated tending to confirm those first impressions. When, finally, Czerny's observation (published in 1883), and König's remarks on operative dissemination of tuberculosis (both published in the *Centralblatt für Chirurgie*, 1884) appeared, the interest of the author was quickened by their strong confirmatory, though indirect, evidence.

They both, like the author, did not advance anything absolutely new, as everybody knows that many patients operated on for joint-tuberculosis died subsequently, and soon after the operation, of meningeal or other forms of disease. But they drew attention to the fact that the *post hoc* might be in many cases also a *propter hoc*.

The author's case in question was as follows:

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[1] Read before the New York Surgical Society February 8, 1885.

I. A., an aged lady, of robust health and a cheerful disposition, presented herself for treatment on account of an elevated ulcer of the outer margin of the sole of her right foot. It had existed for over thirteen years, growing very slowly, until it had attained the size of three inches by two inches and a half in diameter. It was segmented, each segment showing a distinct epidermidal margin, the edges of the ulcer somewhat overlapping the normal skin. While open, the purplish-red ulcer discharged large quantities of a clear serum, but, if the patient refrained from walking, it readily cicatrized over, to become sore again on her using the foot. Previously the pain or inconvenience had been very slight, nor were any glands infiltrated. Lately, however, the sore had become very painful.

Excision was proposed, and carried out in the autumn of 1877, when the base of the new growth was found to be attached to the plantar aponeurosis, which accordingly had to be removed too. The wound healed rapidly by granulation. The diagnosis of granuloma made previous to the operation, and based upon the benign development of the disease, was confirmed on microscopical examination made by Dr. I. Adler, of this city. A favorable prognosis was expressed, and the patient was encouraged to to use her foot. Immediately upon cicatrization being completed, a number of small, purplish, pigmented nodules made their appearance in and about the scar, and well up the leg, increasing daily in number and size. Any doubts about the formidable character of the new growth were dispelled then, and a high amputation of the thigh was at once proposed to, but declined by the patient, who, however, finally submitted to the operation in May, 1878. A mass of enlarged glands was also removed from below Poupart's ligament. Both wounds healed by the first intention, but the operation did not delay the patient's impending fate. A few days after the removal of the limb the patient inquired about the significance of a disturbance of vision which she had noticed for four weeks, but, in her excitement preceding the amputation, omitted to mention to the author. It will suffice to say that a retro-bulbar node, causing first diplopia, finally protruded the eyeball from its socket in a frightful manner, and that the entire body of the patient became covered with innumerable nodes and nodules in an astonishingly short time. The patient's death by suicide fitly closed the tragedy, which did not fail to make upon the author a deep and lasting impression. Post-mortem examination revealed that all the organs, especially the viscera, were permeated with thousands of nodules of pigmented cancer.

Undoubtedly, then, we must have had originally a true granuloma, which at the time of the first operation was undergoing the not unusual change into cancer, some portions of the tumor then removed still presenting the characters of a connective-tissue growth, as Dr. Adler's examination had proved. But is the fact of this change of a benign into a malignant neoplasm alone sufficient to explain its astonishingly swift dissemination? Certainly not, as all processes of dissemination observed in malignant new growths, local and systematic, are notoriously slow, and not to be compared with that in the foregoing case. By "slow" is understood a spread in "*étapes*," as the French say, or marches, to use a strategical term. That is, a modus which is not continuous, but interrupted, and is characterized by well-defined phases of activity and seeming rest.

First comes the simplest and most immediate spread *by contact* with neighboring tissues, which generally lasts for a considerable time, but soon is followed by the second phase—that is, that of the infection of the pertinent *lymphatic vessels and glands.* These serve as a barrier for a certain period of time, till, a large vein becoming involved, transplantation by embolism extends the disease to one or more rather distant organs. This last one would form the *third, or generalizing* phase of infection.

In the case related to you, local and general dissemination seem to have taken place simultaneously, and in a manner closely resembling certain physiological and pathological experiments performed on animals, where substances capable of multiplication are injected into the parenchyma or directly into the circulation. The assumption of a mechanical rapid distribution of the infective bodies is almost imperative, and this rapid mechanical distribution of the infective elements may have been accomplished by the manipulations involved in the performance of the operation.

Observations similar to, if not as striking as, the one related, have multiplied in the experience of the author, extending over forty cases of amputation of the breast done since the year 1878, and the practice of every busy surgeon must yield a not inconsiderable number of instances of the same character. As none of the cases of this character possess the elements of proof positive, it would be unnecessary to weary your patience by records of similar cases, but it is important to tell you that the practical wisdom of an older generation of surgeons has impliedly admitted the truth of our assumption by advising amputation of an extremity affected by what was then termed "cancer," in preference to a mere extirpation of notoriously malignant growths. And the value of this advice is twofold: first, it more fully eliminates all foci of disease than an excision, however comprehensive; and, last, but not least, the field of operation being more or less distant from the seat of the disease, handling of the tumor and manipulative dissemination of its elements are less likely to occur than otherwise.

Now let us consider what amount of force and energy is employed in the handling of tumors by physicians, and whether this handling does not possess some or all the characters of that form of manipulation which the French denote as "massage."

A careful physical examination of the tumor, especially if made by the aid of anæsthesia, will be, and notoriously is, frequently accompanied by the use of a good deal of necessary or unnecessary force. The handlings or manipulations ordinarily in use during the performance of bloody operations on tumors to be dissected out of surrounding tissues have positively the character of massage, and occasionally a very rough form of massage, too. And the employment of anæsthetics has certainly not had the effect of increasing the gentleness of operative interference. Suffice it to say that the manipulation employed on a tumor of the breast and the lymphatic glands occupying the adjacent axillary cavity, during an operation lasting one or two hours, certainly may have the dignity of a manipulative *séance*. And all of you know that a skillful massage of thirty minutes will often cause a massive extravasation of blood to disappear from the vicinity of a sprained joint, and that three or four sittings may dispel the largest part of a solid infiltration of an inflammatory character from this or that part of the body. Now, just bear in mind how many formed corpuscular elements, be they cells or broken-up portions of a firm clot, must be propelled through the lymphatics and veins into the general circulation at each massage, and the idea of the probability of the propulsion of cancerous elements of an unfixed, minute (that is, embryonic) character, and situated especially in recently involved places about the margins of a tumor, is very plausible indeed. The analogy of these artificial processes is *a priori* evident, and the fact that mechanical irritation—that is, another form of massage—favors the spread of malignant disease, stands fully in accord with this assumption. Finally, it seems appropriate to adduce here Billroth's authority as a pathologist in these his words: "I consider it most highly probable that both the continuous and the discontinuous spread of carcinomata are effected (*vermittelt*) by the dissemination of corpuscular elements, but admit that, so far, we are unable to prove this in all cases."[1]

The author does not wish to have it understood as though he considered this mode of dissemination the rule, but he believes that in a number of cases of malignant disease operative treatment may hasten rather than retard death. This statement seems to contradict the results of statistical investigation as laid down by such authorities as von Winiwarter and Gross, whose meritorious works are well known to all surgeons.

But this contradiction is partial only, and is justified by the nature of statistical results in general, which we know are arrived at by summing together cases widely different in character, though all representing the same disease.

Our critical attention will necessarily be first directed to the comparative estimates by averages of the duration of life of patients operated on for cancer of the breast and patients not subjected to operative treatment.

Here we see that Winiwarter finds the average duration of life from the beginning of the disease of the patients operated on to be about 39.5 months, whereas that of patients left to their fate is almost 33 months. The former, accordingly, live on an average about six months and a half longer than those not coming under the surgeon's knife.

On further examining the figures it will be remarked at once, that the number of observations of non-operated cases is very small as justly compared with those operated on, one being 97, the other 519. Take into consideration, furthermore, that many, if not all, of the non-operated cases were subjected to all manner of irritative treatment, greatly influencing their rapid development and dissemination; finally, that many of them may have been such as show a formidable malignant character, deterring even the boldest operator, and it will be easy to comprehend that the rate of mortality as calculated for these 97 cases is unreliable and too high if applied to all cases of unoperated cancer, many of which, not being very malignant, did not come under operation at all. But let us analyze the class comprising those subjected to operation. Here we find that somewhat over *nine per cent.* of the cases were permanently cured by the operation. They necessarily must have been those in which a complete removal of all diseased tissues was successfully accomplished. It is of the utmost importance to note that such a thing is possible under certain most favorable conditions, offered by an early and very thorough operation upon a not extensive tumor of comparatively slow growth. Clinicians know and admit differences of infectiousness in cancers, which depend upon a more or less rapid growth, and accordingly upon a greater or less proportion of succulency attributable to more or less embryonic, non-fixed, or movable tissue components or corpuscular elements. Their anatomical expression is a greater or lesser proportion of *cancer juice*, as produced by scraping of their cut surface with a scalpel.

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[1] "*Deutsche Chirurgie; Krankheiten der Brustdrüsen*," p. 112.

To go back to a former comparison, we may say that, as the corpuscular or liquid elements of a recent succulent inflammatory infiltration are more easily dispersed by massage, so will the elements of a succulent cancer be more prone to be dispersed by mechanical factors, and we may add that their rapidity of reproduction also stands in direct proportion to the ease with which they are dispersed. This relationship suggests resemblance to a geometrical progression, and may serve to explain the enormous differences of malignity observed in cases standing at the foot and at the head of the statistical scale respectively. Gross mentions a case that terminated fatally without operation at the expiration of five months. Billroth gives the history of one in which the patient lived for twenty years.

To return to the cases cured permanently, we may say that a few of them may have been very malignant ones, operated upon very early and very radically, but that most of them were not very malignant and were subjected to a very radical operation; finally, that in all of them up to the patient's death from other diseases no formation of cancer, *de novo*, had taken place. (It is still a mooted question whether even a regional recurrence of cancer three or more years after operation is a continuation of the old process, or a new disease, *per se.*)

The large majority of the three hundred and sixty-eight cases operated upon, that is, nearly eighty-one per cent., showed recurrence. In eleven and a half per cent. of the three hundred and sixty-eight cases, recurrence took place after twelve months; but it does not appear in what manner or where. It would be important to find whether the general character of these recurrent tumors was mild or severe, local or general, and what was their microscopical nature (succulent or firm and dry).

Presumably these were mostly tumors of not great malignancy or of a slow growth, incompletely removed, yet so that very few cancerous elements were left behind to multiply.

It may be pertinent here to mention the curious fact, though no explanation of it is ventured, that seemingly infected glands have been seen to disappear after the removal of the primary tumor in such cases even where the knotty, hard nature of the glandular swelling fully justified the assumption of its cancerous character.

Within three months sixty-three per cent. of the cases relapsed, forty-three per cent. within *four weeks*, and nineteen per cent. even before the lapse of a *fortnight*.

In about eighty-two per cent. of one hundred and ninety-four cases of recurrent cancer where this point was noted, the locality of the relapse was in the cicatrix, in the remains of the mamma or in its vicinity, and in the glands.

These figures are appalling; they show that in almost two-thirds of all cases operated upon relapses are established within three months after the operation. Undoubtedly the great majority of these cases represent very incomplete operations, where already disseminated portions of the neoplasm were left behind, either in the vicinity of the primary growth or in or about infected lymphatic vessels and glands. The cases relapsing within four weeks (43 per cent.), and still more so those recurring within a fortnight (19 per cent.), must be those in which either grossly incomplete operations were performed, or artificial operative dissemination took place, or finally where both of these occurrences combined to cause a rapid involvement of hitherto seemingly healthy tissues. We have to add, finally, while treating of this group, a class of cases characterized by Billroth in the following words: "Cases operated on under seemingly very favorable circumstances—in which, however, the patients are already victims of internal carcinosis, this becoming evident on post-mortem examination made soon after the operation—are, unfortunately, *not very rare.*[1]

Of course the occurrence of such cases can not be gainsaid, but, considering the gradual extension of cancer observed as a rule, such an infection by a jump, as it were, must nearly always be caused by mechanical factors. By these are meant either a build and arrangement of the lymphatics unusually favorable for the easy transmission of corpuscular elements, or a very energetic and effective external agency, such as a traumatism, or massage, or long-continued compression, or all of these combined.

But, to return to our subject, we will say that von Winiwarter does not state whether a change in the character of the malignancy of these neoplasms was observed or not on their recurrence after operation. And herein all observations are strangely defective, and unfortunately so, as this seems to constitute the nodal point of our inquiry. If it were shown that in a certain number of tumors of previously slow growth a fast and extensive *local* recurrence took place immediately after a comprehensive and thorough-going operation, performed by a competent and experienced surgeon, it would be necessary to assume the concurrence of a factor hitherto unknown, even unthought of. And if the marginal portions of the removed

[1] *Loc. cit.*, p. 117.

tissues were found, on careful and exhaustive examination, to be entirely free from such miliary foci of cancer as can be detected by the microscope, the presumption of a direct influence upon the nature and course of the disease by the operation would be almost imperative.

Older surgical writers directly admit the possibility of such an influence; modern authors, as, for instance, Billroth and Volkman, only by inference; and their reticence in this respect is easily explained by the lack of a sufficiently large sum of observations collected with a view to the ascertainment of this very point, and by the necessity of questioning the correctness of the generally accepted assumption that the operated cases show a much longer average duration of life than those let alone.

Let us now examine what this peculiar "influence" of operative or other mechanical irritation upon a cancerous growth may consist in. Excluding chemical irritation, and considering only forms of irritation looked upon as more strictly mechanical and akin to massage, we find that this influence may be twofold. On the one hand, it may induce active hyperæmia, a better nutrition of the tumor, and hence a more rapid multiplication of existing elements *in situ*. On the other hand, and following from the first, it will increase the activity of the lymphatics, and fitly prepare them for the reception and transmission of mobile cancerous elements. Finally, the changing degrees of pressure from different sides, and its intermittent character will not fail in suitable cases to propel such cancerous elements to a shorter or longer distance; and, if the form of mechanical irritation is constant or frequent, a large area of the surrounding tissues may become injected with cancerous elements in a comparatively short time. Supposing that all this takes place during an operation, followed by unavoidable stimulation of the tissues thus infected incumbent upon the processes of repair, what wonder if we see a large number of small nodes appear in and about the cicatrix left after the removal of a solitary tumor, and within a few weeks after the operation?

Instead of assuming a mysterious, indefinable change in the character in the new growth, it is more rational to explain a natural process by natural and well-known biological laws. It may be objected that all operations followed by a rapid and wide-spread reappearance of the disease about the sites operated on must be those in which pre-existing foci of cancer were unwittingly left behind by the operator. Admitting, as we have done before, that a large number of cases are covered by this explanation, yet we may reply to this with the following question: What is the reason, then, of the simultaneous appearance and rapid growth of a large number of cutaneous foci shortly after the operation on a formerly slowly growing tumor? Why do these foci remain dormant, or grow imperceptibly until the time of the operation, and suddenly come forward in an unmistakable manner after the traumatism of an operation? And there is not only a spread, there is frequently also an increased rapidity of the multiplication of the elements, an increased malignity denoted as a *change of character*. And why this? Our explanation seems to cover these questions.

Besides, it is not impossible that young cancerous cells, sown, as it were, in new soil, well prepared by an increased blood-supply due to the healing process, will thrive much better in this unexhausted, well-irrigated ground than elsewhere.

Of course all this does not prejudice the acceptance of the fact that positively benign tumors do change occasionally into malignant ones, but it seems that this important mechanical factor in the growth and dissemination of cancer ought to receive some recognition.

The author has begun a series of experiments tending to prove the possibility of mechanical or surgical dissemination. But the results of the investigation of the subject have not matured yet for publication. Before completing this paper it may be appropriate to point out in a few words its practical bearings.

It is not intended to question the general correctness of the advisability of operating even in far-gone cases of cancer. On the contrary, it is hoped that by pointing out one more danger we may be taught to avoid this also, and thereby the results of operative measures in this field may become better. Antiseptic treatment has here, too, undoubtedly stimulated active surgical interference, and, though the author's material includes only thirty-four cases of malignant tumors of the breast operated upon radically—that is, in which the breast and the axillary contents were removed, and six partial operations, with no deaths resulting from the operations—this may justify the conclusion that antiseptic measures must have generally depressed the death-rate of 16.5 per cent., as given by Winiwarter.

Nothing need be said about the necessity of early operations, and the very radical, extensive removal of a wide zone of seemingly healthy tissues surrounding a cancroidal tumor. If the neoplasm is on an extremity and is extensive, the preference should be given to an amputation done far away from the disease. Wōlfler has conclusively shown on animals that, during the time that Esmarch's constriction is applied to a limb, the veins and lymphatics beyond the constricting band are inactive, and do not absorb even soluble substances, and that these do not enter the ostia of the vessels opened by the surgeon's knife as long as the constriction lasts.[1] It seems to be rational, then, to always employ Esmarch's constriction while excising malignant tumors situated on a limb, since it is improbable that corpuscular elements would be propelled where there is no medium, such as blood or lymph, to carry them along. In examining any kind of tumor, the utmost gentleness should be observed, and obscure points in the diagnosis not bearing upon the therapy should rather be left undecided till after the operation. Unnecessary handling of a suspicious tumor should be discouraged, and the patients especially warned against so-called abortive methods of treatment, as painting with irritating chemicals, and especially the several forms of compression, constant or interrupted.

As a preparatory measure, the hyperæmia and cell-activity of a rapidly growing tumor should be reduced as much as possible by the constant application of ice, or the water coil, for several days preceding the operation, as it is notorious that the growth of some tumors has been noticeably retarded by the influence of low temperatures.

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[1] *Archiv. für klin. Chirurgie*, 27 Band, p. 413.

During the exsection of deeply imbedded tumors all rough handling, pulling to and fro, should be avoided as much as possible. This may be very difficult in cases of large, heavy tumors, or where it is necessary to work in a deep, non-dilatable wound, wherefore the proposal of an English surgeon to fasten into each tumor, after its exposure, a sharp hook attached by rope and pulley to the ceiling of the operating-room, seems to be very appropriate. One assistant can easily raise or lower even a very large tumor by traction applied to the rope running through the pulley, while the surgeon himself, holding the shank of the hook, can carry out without fatigue such lateral movements as become necessary in the course of the operation. This would deserve a trial, especially in amputations of the female breast. For self-evident reasons the axillary fat should be invariably removed, and in one mass, this being much easier and safer than the digging out of single glands. The operation should be begun, if possible, with the evacuation of the axillary space, and its contents, together with the breast and the intervening tissues, should be removed in one piece.

Primary union of the entire operation wound should be always aimed at where possible, since suppurative processes and the increased reproductive activity of the tissues depending thereon tend to cause an early development of such cancerous elements as may have been left behind.

The view that non-destructive suppuration may eliminate such cancerous elements has no support in pathology. The surgeon should rather use his knife freely than invoke the aid of such a treacherous ally as suppuration.